Original Article

Effects of intraoperative inverse ratio ventilation on postoperative pulmonary function tests in the patients undergoing laparoscopic cholecystectomy: A prospective single blind study

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ABSTRACT

Background and Aims: Induction of general anaesthesia is associated with development of atelectasis in the lungs, which may further lead to postoperative pulmonary complications. Inverse ratio ventilation (IRV) has shown to improve oxygenation and minimise further lung injury in patients with acute respiratory distress syndrome. We evaluated the safety and effectiveness of IRV on intraoperative respiratory mechanics and postoperative pulmonary function tests (PFTs). **Methods:** In a prospective, controlled study, 128 consecutive patients with normal preoperative PFTs who underwent elective laparoscopic cholecystectomy were randomised into IRV and conventional ventilation groups. Initially, all patients were ventilated with settings of tidal volume 8 mL/kg, respiratory rate 12/min, inspiratory/expiratory ratio (I: E) = 1:2, positive end expiratory pressure = 0. Once the pneumoperitoneum was created, the conventional group patients were continued to be ventilated with same settings. However, in the IRV group, I: E ratio was changed to 2:1. Peak pressure (Ppeak), Plateau pressure (Pplat) and lung compliance were measured. Haemodynamic parameters and arterial blood gas values were also measured. PFTs were repeated in postoperative period. Statistical tool included Chi-square test. **Results:** There was no significant difference in PFTs in patients who underwent IRV as compared to conventional ventilation [forced vital capacity (FVC) 2.52 ± 0.13 versus 2.63 ± 0.16, $P = 0.28$]. The Ppeak (cmH2O) and Pplat (cmH2O) were statistically lower in IRV patients [Ppeak 21.4 ± 3.4 versus 22.4 ± 4.2, $P = 0.003$] [Pplat 18.7 ± 2.4 versus 19.9.4 ± 3.2, $P = 0.008$]. There was no significant difference in lung compliance and oxygenation intraoperatively. **Conclusion:** Intraoperative IRV led to reduced airway pressures; however, it did not prevent deterioration of PFTs in postoperative period.

Key words: Atelectasis, general anaesthesia, inverse ratio ventilation, laparoscopic cholecystectomy, lung protective ventilation, postoperative pulmonary complications

INTRODUCTION

General anaesthesia with neuromuscular blockade and controlled ventilation is now known to be a major cause of respiratory impairment in the postoperative period. Induction of general anaesthesia itself is associated with altered respiratory mechanics with reduced lung volumes and atelectatic zones formation.[1]

Laparoscopic cholecystectomy has become a standard of care recently. Laparoscopic surgery requires insufflation

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of intra-peritoneal gas to create space for visualisation and surgical manoeuvres. During laparoscopic abdominal surgeries, changes in respiratory mechanics are even further exaggerated due to splinting effect of pneumoperitoneum on diaphragm.[2]

Protective lung ventilation strategies have been reported to be useful to reduce the respiratory complications in the postoperative period. The use of small tidal volume, positive end expiratory pressure (PEEP) and restricting peak airway pressure (Ppeak) have shown to reduce the incidence of ventilation-induced lung injury (VILI). Restriction of Ppeak, alveolar recruitment, improving oxygenation, thus minimising VILI may also be achieved with inverse ratio ventilation (IRV).[3,4] However, the potential utility of IRV has not been much studied in patients undergoing surgeries under general anaesthesia**.**

We hypothesised that in patients with normal preoperative lung functions scheduled for elective laparoscopic cholecystectomy, IRV might prevent deterioration of pulmonary function in the postoperative period. We compared the IRV and conventional ventilation on oxygenation, intraoperative respiratory mechanics and postoperative pulmonary functions in patients scheduled for elective laparoscopic cholecystectomy.

METHODS

This was a randomised, single-blind study, done in the Department of Anaesthesiology of our institute over a period of 1 year. The study protocol was approved by the Institutional Ethical Committee. The study protocol was registered at clinicaltrials.gov. Written informed consent was obtained from all the participants. 128 patients who underwent laparoscopic cholecystectomy in 1-year (2017–2018) duration were included in the study. One hundred twenty-eight patients (n = 128) were randomly assigned into 1:1 ratio to receive IRV or conventional mechanical ventilation. Patients of American Society of Anesthesiologists(ASA) physical status grade I–II, aged between 18–60 years and undergoing elective laparoscopic cholecystectomy were included in the study. Patients with significant pulmonary disease, significant cardiac dysfunction and body mass index (BMI) >30 kg/m^2 were excluded from the study. Consecutive patients planned for elective laparoscopic cholecystectomy within the 1 year were recruited for the study.

Preoperative pulmonary function tests (PFTs) were done by using HELIOS 401 spirometer for all the patients participating in the study one day prior to surgery. Values of FVC, forced expiratory volume in 1 s (FEV1), and forced expiratory flow 25%–75% (FEF 25%–75%) were recorded. All the patients were kept fasting for solids for at least 8 h prior to the surgery. The patients received premedication in the form of oral ranitidine 150 mg and alprazolam 0.25 mg in the night before and on the morning of the surgery.

Upon arrival in the operating room, standard monitors like electrocardiogram, heart rate (HR), pulse oximetry (SpO2), and non-invasive blood pressure (NIBP) were attached. Peripheral intravenous (IV) access was secured and IV fluid connected. Arterial blood gas analysis (ABG) was done at room air as baseline and partial pressure of oxygen in arterial blood and fraction of inspired oxygen (PaO2/FiO2) ratio was calculated. Anaesthesia was induced with IV fentanyl (1–2 μg/kg), propofol (1–2 mg/kg) and vecuronium (0.1 mg/kg). Neuromuscular monitoring (NMT) was applied following induction of anaesthesia. Patients were mask ventilated till train of four (TOF) ratio value was 0. Direct laryngoscopy was done and patients were intubated with polyvinyl chloride endotracheal tube. Correct position of tube was confirmed. Anaesthesia depth was monitored with bi-spectral index monitoring and maintained within values between 45-55. NMT was continued intraoperatively and intermittent top-ups of vecuronium were administered according to TOF ratio. Anaesthesia was maintained with oxygen (33%) with nitrous oxide (77%), sevoflurane, intermittent top-ups of vecuronium (0.05 mg/kg) and analgesia was maintained with 0.5 μg/kg/h bolus of fentanyl. Patients were mechanically ventilated using Drager primus infinity C700 Anaesthesia workstation.

Group 1 (conventional) patients received conventional ventilation throughout the surgery with ventilatory settings of tidal volume of 8–10 mL/kg, respiratory rate of 12/min, inspiratory: expiratory ratio of 1:2 and PEEP = 0. Group 2(IRV) patients initially received same conventional ventilation as in group 1. However, once the pneumoperitoneum was created, the inspiratory/expiratory (I: E) ratio changed to 2:1 until the completion of surgery. If Ppeak increased to >30 cm H20, ventilatory parameters were altered to maintain Ppeak <30 cm H20 and such incidences were noted. Intra-abdominal insufflation of carbon dioxide was done @4–6 L/min and intra-abdominal pressure was maintained in physiological limits of 10–15 mmHg throughout the procedure in both the groups.

Haemodynamic parameters, such as systolic blood pressure (SBP), diastolic blood pressure (DBP), HR and SpO2, were recorded as baseline and at 5 min, following induction, then at every 15-min interval throughout the surgical procedure. Ppeak, Pplat, dynamic lung compliance (tidal volume/Ppeak) and end tidal carbon dioxide (EtCO2) were recorded at 15-min intervals. EtCO2 was kept between 35 and 45 mmHg. Patients were given inj. diclofenac (1 mg/kg) IV and inj. ondansetron (0.1 mg/kg) at the end of surgery. Patients were reversed and extubated at the end of surgery.

Following surgery, patients were shifted to postanaesthesia care unit (PACU). Oxygen was supplemented with face mask and ABG analysis was done 30 min later. On the first postoperative day, visual analogue scale (VAS) pain score was recorded. Once VAS was ≤4, PFTs were performed at the bedside with patient seated in comfortable position. Our primary objective was to compare the intraoperative oxygenation and PFTs postoperatively. Our secondary objective was to compare intraoperative respiratory mechanics and haemodynamics.

Continuous variables like age, weight, BMI, HR, SBP, DBP, SpO2 and ABG values were presented as mean ± standard deviation (SD) with 95% confidence interval and analysed with student's *t*-test or Mann–Whitney *U* test as appropriate. The qualitative data were analysed by using Chi-square/Fisher test as appropriate. Data analysis was done by using the statistical software package Statistical Package for the Social Sciences (SPSS) (International Business Machines) version 20.0. $P \leq 0.05$ was considered statistically significant.

RESULTS

A total of 135 patients were assessed for eligibility. Six ($n = 6$) patients were excluded based on exclusion criteria. One ($n = 1$) patient denied participation in the study. A total of 128 patients were included in this study and they were randomly assigned to group 1 ($n = 64$) and group 2 ($n = 64$). Among 64 patients in Group 1, three patients ($n = 3$) were excluded from the study as the laparoscopic surgery was converted to open surgery. In group-2, one patient ($n = 1$) was excluded from the study as the patient developed significant bronchospasm following intubation leading to Ppeak >30 cm H20. After evaluating history again in the postoperative period, patient was diagnosed to have reactive airway due to recent upper respiratory tract infection. A total of 124 patients were analysed at the end of study [Figure 1].

The two groups were comparable with respect to demographic variables [Table 1]. Haemodynamic parameters were comparable at all stages of surgery between the two groups. Surgery duration was also comparable between the groups [Table 1].

There was no significant difference in haemodynamic parameters between the two groups, such as SBP, DBP, and HR, at all the points. Ppeak was statistically higher in Group 1 as compared to Group 2 following creation of pneumoperitoneum [21.67 ± 3.12 cm H2O {Group 1} versus 20.30 ± 2.53 cm H2O {Group 2} ($P = 0.003$)] [Table 2]. Dynamic lung compliance decreased significantly ($P < 0.05$) in both the groups following pneumoperitoneum. However, dynamic compliance was not significantly different between the groups, at all the time points [Table 2].

PaO2/FiO2 ratio was reduced in postoperative period as compared to baseline value (preinduction) in both the groups; however, it was not significantly different in between the groups [Table 3]. There was no significant difference in the PaCO2 levels in both the groups. PFTs (FEV1, FVC, and FEF25%–75%) were also not significantly different in between the groups postoperatively. However, PFTs were significantly reduced in both the groups postoperatively as compared to preoperative values ($P = 0.001$) [Table 4]. There were no pulmonary complications in both the groups postoperatively.

DISCUSSION

In this study, use of IRV intraoperatively led to reduced airway pressures; however, we did not find any significant difference in oxygenation, ventilation and postoperative PFTs in between the groups.

Table 1: Baseline characteristics of patients

Parameters	Group: 1 (*n*=61)	Group: 2 (*n*=63)	*P*
Age (years)	38±10	41±9	0.15
Weight (kg)	59±10	61±10	0.52
Height (cm)	157±6	159±8	0.20
BMI (kg/m^2)	22.8±2.2	24.0±2.4	0.20
Duration of surgery (min)	34.09±9.18	34.42±9.38	0.88
Duration of anaesthesia (min)	39.63±9.20	40.33±8.63	0.75

*BMI=body mass index

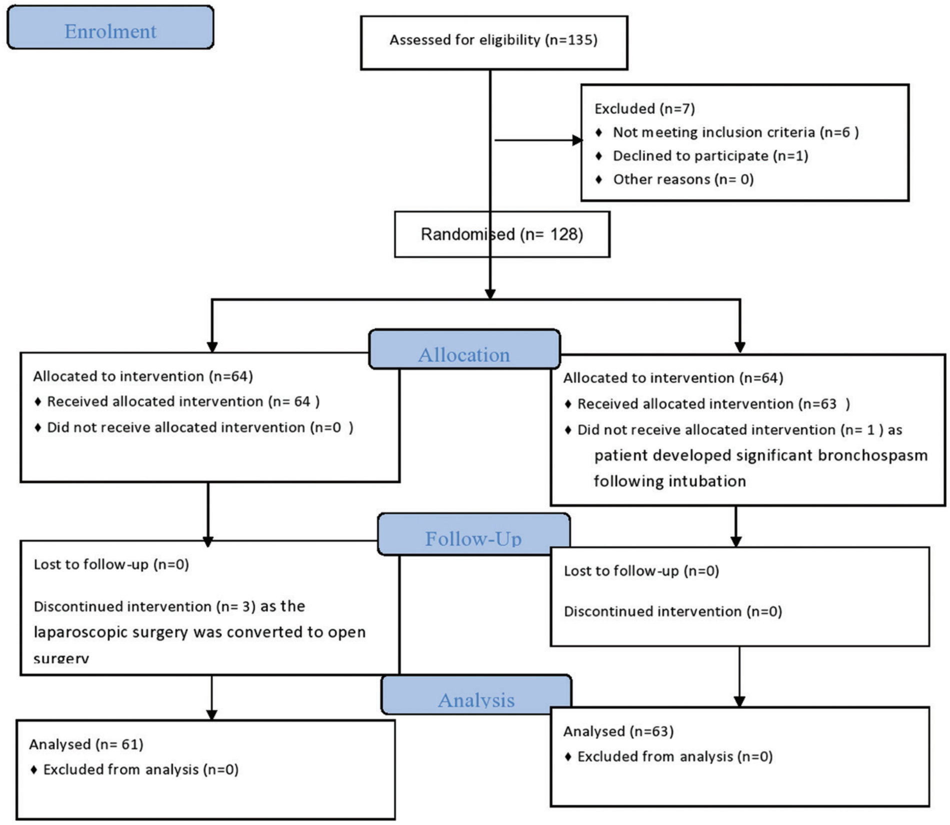

Figure 1: CONSORT flow diagram

Table 2: Intraoperative respiratory parameters in both the groups

	T0 (immediately after induction)	T1 (5 min after CO_2 insuff)	T2 (15 min after CO_2 insuff)	T3 (30 min after CO_2 insuff)	*P*
Peak airway pressures (mmHg)					
Group 1 (*n*=61)	13.9±2	21.6±3.1	21.7±3	21.6±3	<0.001
Group 2 (*n*=63)	13.8±2.2	20.2±2.5	20.2±2.3	20.2±2.4	<0.001
P	0.66	0.003*	0.087	0.002*	
Dynamic lung compliance					
Group 1 (*n*=61)	33.7±6.3	21.4±3.4	21.3±3.4	21.4±3.6	0.001
Group 2 (*n*=63)	34.0±6.6	22.4±4.2	22.4±4.0	22.4±4.0	0.001
P	0.122	0.137	0.087	0.134	
Plateau airway pressure (mmHg)					
Group 1 (*n*=61)	12.4±2.3	19.9±3.2	19.9±3.3	19.3±3.2	0.001
Group 2 (*n*=63)	12.4±2.0	18.7±2.4	18.8±2.4	18.9±2.5	0.001
P	0.84	0.008*	0.052	0.430	

During laparoscopic surgery, as the intra-abdominal pressure increases with pneumoperitoneum, it leads to decrease in lung compliance, diminution of lung volumes and increased airway pressure.[5] These changes in respiratory physiology can be partially reversed with the use of IRV.[6] IRV increases the mean airway pressure (Pmean), recruits atelectatic alveoli, reduces intrapulmonary shunt, improves ventilation–perfusion matching and decreases the dead space ventilation.[7] Secondly, increased inspiratory time may provide enough time for gaseous exchange, mainly oxygen effectively.[7] Despite all these facts, we did not find any significant difference in postoperative PFTs in between the groups. It may be due to the fact that patients included were having healthy lungs, surgery was done in reverse Trendelenburg position and average surgical duration was quite short (30 ± 10 min). Postoperative pain intensity plays a major role in preserving pulmonary function after surgery.[8] Patients with severe pain in abdominal surgeries tend to have shallow breathing, which may further increase lung atelectasis and deteriorate

Table 3: Blood gas analysis of two groups

	T0 (preinduction)	T1 (30 min)	T2 (post op)	*P*
PaO_2/FiO_2 ratio				
Group 1 (*n*=61)	497±70	508±72	470±76	0.001
Group 2 (*n*=63)	487±77	495±84	460±60	0.001
P	0.168	0.73	0.519	
$PaCo_2$				
Group 1 (*n*=61)	35.1±2.6	38.5±5.2	34.2±4.3	0.22
Group 2 (*n*=63)	34.4±2.4	36.7±3.7	34.1±2.6	0.21
P	0.23	0.24	0.38	
$EtCo_2$				
Group 1 (*n*=61)	32.4±1.6	34.6±4.3		
Group 2 (*n*=63)	32.1±2.1	33.8±2.3		
P	0.37	0.19		

PaO_2=Partial pressure of oxygen in arterial blood, FiO_2=Fraction of oxygen in inspired oxygen, $PaCO_2$=Partial pressure of carbon di oxide in arterial blood, $EtCO_2$=End tidal carbon di oxide

Table 4: Postoperative pulmonary function tests

	Group 1 (*n*=61)	Group 2 (*n*=63)	*P*
FEV1			
Pre op	2.40±0.23	2.49±0.2	0.449
Post op	2.34±0.17	2.26±0.17	0.156
FVC			
Pre op	2.71±0.21	2.80±0.30	0.55
Post op	2.52±0.13	2.63±0.16	0.28
FEV 25-75			
Pre op	2.51±0.19	2.56±0.21	0.512
Post op	2.28±1.34	2.30±0.12	0.53
P	0.001	0.001	

FEV1=Forced expiratory volume in one second, FVC=Forced vital capacity, FEV=Forced expiratory flow at 25%-75% of the pulmonary volume

ventilation perfusion mismatch postoperatively. In our study, the VAS pain score was comparable between the two groups.

Statistically, lower Ppeak and Pplat were observed in IRV group as compared to the control group; however, clinically, the difference was marginal. Lower Ppeak and Pplat in IRV group was possibly because of the longer inspiratory time or slow inspiratory flow.[9] IRV decreases the Pplat, increases Pmean and may alleviate the inflammatory response thus reducing all forms of acute lung injury.[7] In our study, no external PEEP was applied and we found no evidence of intrinsic PEEP. This finding is consistent with the previous studies where there is no evidence of auto PEEP generation during IRV application in laparoscopic surgeries.[7] Hossein *et al*. compared pressure-controlled IRV and pressure-controlled ventilation modes in patients undergoing laparoscopic cholecystectomy using laryngeal mask airway (LMA) and concluded that the Ppeak, SpO2 and oxygenation were better with PCIRV group and the results were matching with our study.[10] Zhang *et al*. compared volume-controlled IRV with PEEP and conventional ventilation in 60 patients with lung cancer who underwent pulmonectomy and concluded that IRV could improve hypoxaemia, promote oxygenation, and improve dynamic compliance of respiratory system, moreover reducing Pplat and the release of inflammatory cytokines in patients during one-lung ventilation. It was superior to the conventional ventilation with PEEP during one-lung ventilation.[11] Wang *et al*. compared volume-controlled ventilation with pressure-controlled IRV (PIV) during open abdominal surgery and concluded that PIV improves respiratory compliance, and leads to better pulmonary function test results on first postoperative day.[12]

There was no significant difference in the dynamic compliance in between the groups. However, we observed better dynamic compliance in the IRV group (22.4 ± 4.0) as compared to conventional group (21.4 ± 3.6). It is consistent with the previous studies that increasing the percentage of inspiratory time had improved the lung compliance and oxygenation as compared to the conventional mechanical ventilation.[11] Similar findings were observed in the study conducted in gynaecological laparoscopic surgeries using IRV.[7]

IRV did not affect haemodynamics adversely in this study. It is consistent with the previous statement that increasing the percentage of inspiratory time had no demonstrable changes in haemodynamics during mechanical ventilation.[13] Various studies have shown that only an I: E ratio >2.0 decreases cardiac output.[14] Chronic obstructive pulmonary disease (COPD) is the commonest co-presenting pulmonary disease in our institute. Patients with COPD have extensive expiratory time, that is why they were not included in our study.

Our study had certain limitations such as the contrast-enhanced computed tomography or magnetic resonance imaging chest was not done postoperatively because of financial constraints and ethical issues. This radiological imaging is standard for the diagnosis of postoperative atelectasis. These imaging techniques might have been able to show the atelectatic zones, which were not reflected clinically. Lung injury biomarkers were not measured because of financial concerns which would have supported the results.

In conclusion, intraoperative use of inverse ratio ventilation might decrease the barotrauma by reducing Ppeak in patients undergoing laparoscopic cholecystectomy without affecting haemodynamics adversely.

Future research is required during prolonged surgeries done in obese patients or patients with compromised lungs and prolonged surgery done in head down position.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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